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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/955,585	09/19/2001	Ali I. Fattom	018861-0216	8124

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EXAMINER	
DUFFY, PATRICIA ANN	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 04/07/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/955,585	FATTOM ET AL.	
	Examiner	Art Unit	
	Patricia A. Duffy	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) *4-10 and 13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,11,12 and 14-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-19* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *Aug 12, 03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The response filed January 5, 2004 has been entered into the record.

Specification

The disclosure is objected to because of the following informalities: the specification at page 11 a particular US patent Application. If the Application has been issued as a patent or abandoned, the specification must be updated in regard to the status of this application for which Applicants rely upon. Appropriate correction is required.

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

Information Disclosure Statement

The information disclosure filed August 12, 2003 has been considered. A initialed copy is enclosed.

Election/Restrictions

Applicant's election with traverse of Group I in the Paper filed January 5, 2004 is acknowledged. The traversal is on the ground(s) that all the inventions are in the same class and subclass and that no evidence of separate status in the art or separate field of search is presented for demonstrating a separate field of search. This is not found persuasive because First, the classification system has no statutory recognition whether inventions are independent and distinct. For example, each class and subclass is comprised of numerous completely independent and distinct patented inventions. Second, MPEP 803 states that restriction is proper between patentably distinct inventions where the inventions are (1) independent or distinct as claimed and (2) a serious search and examination burden is placed on the examiner if restriction is not required. The term

"distinct" is defined to mean that two or more subjects as disclosed are related, for example, as product and method of use, etc., but are capable of separate manufacture, use or sale as claimed, and are patentable over each other (see MPEP 802.01). In the instant situation, the inventions of the Groups re drawn to distinct inventions which are related as separate products capable of separate manufacture, use or sale as described in the previous Office Action. Restrictions between the inventions is deemed to be proper for the reasons previously set forth. In regard to burden of search and examination, MPEP 803 states that a burden can be shown if the examiner shows either separate classification, different field of search or separate status in the art. Classification of subject matter is merely one indication of the burdensome nature of search. The literature search, particularly relevant in this art, is not co-extensive, because, for example, *Staphylococcal* polysaccharide antigens are chemically distinct from Enterococcal antigens. Further, the claims specifically require the presence or absence of O-acetyl groups. As such, a search for the presence of a particular chemical structure in the is case would necessarily exclude the absence of such a structure and as such, these searches are not co-extensive. Further, it is submitted that the inventions of Groups have acquired a separate status in the art because there is no cross-protection between Staphylococcus and Enterococcus. The claims define use of patentably distinct different chemical structures derived from different genus and species of bacteria to the extent that no-coextensive searches can be applied. Further, the examination issues with respect to vaccine are particular to each microorganism, Clearly different searches and issues are involved in the examination of each Group as set forth.

For these reasons the restriction requirement is deemed to be proper and is therefore made FINAL.

Claims 4-10 and 13 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or

linking claim. Applicant timely traversed the restriction (election) requirement in the Paper Filed January 5, 2004.

Claim Objections

Claims 2, 3, 11 and 12 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The elected invention was drawn to Markush member (a) which recites the vaccine comprises glycoconjugates of both Type 5 and Type 8 polysaccharide antigens of Staphylococcus aureus. Claim 2 clearly broadens the scope of claim 1 because it recites that the vaccine comprises at least one of Type 5 and Type 8 and as such is seen to broaden the scope of the claims by claiming less than that of the independent claim. As to claims 3, 11 and 12, the recitations of the claim do not further limit the elected invention a method of vaccinating comprising administering a vaccine comprising Markush member (a). Correction is required.

Claims 1, 11, 12, 14-19 are objected to under 37 CFR 1.75(c) as being in improper form because they include non-elected subject matter. Correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 3, 11, 12, 14-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of protecting an immune-compromised end stage renal disease human patient from an infection by *Staphylococcus aureus* comprising administering a vaccine comprising a glycoconjugate of a polysaccharide and an immunocarrier to the patient wherein the vaccine comprises glycoconjugates of both Type 5 and Type 8 polysaccharide antigens of *Staphylococcus aureus* and optionally an adjuvant, it does not reasonably provide enablement for protection of cancer patients, AIDS patients, diabetic patients, elderly, patients on immunosuppressive therapy, transplant patients, patients with surgical procedures, burn patients and other patients in acute care settings. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The dictionary definition of vaccine is "A prophylactic or therapeutic material containing antigens derived from one or more pathogenic organisms which, on administration to man or animal, will stimulate active immunity and protect against infection with these or related organism (i.e. produce protective immunity)." (The Dictionary of Immunology, Herbert et al eds, Academic Press, 1995). Fattom et al (Annals of Medicine, 28:43-46, 1996; reference A3 on PTOL-1449) teaches that "Staphylococci are therefore considered to be opportunistic pathogens. Thus, *S. aureus* vaccines would probably not be intended for use for mass immunization. Rather such vaccine would be used to prevent staphylococcal infections in certain high-risk populations. Renal disease patients on dialysis, HIV infected patients and individuals with scheduled high-risk surgery

who are capable of mounting an immune response are likely to benefit from active immunization. On the other hand, active immunization is unlikely to work in low birth weight neonates, or cancer, AIDS, and burn patients who are strongly immunocompromised." (page 45, column 2, lines 5-25). The specification fails to teach that other severely immunocompromised patients such as the claimed cancer patients, AIDS patients, diabetic patients, elderly, patients on immunosuppressive therapy, transplant patients, patients with surgical procedures, burn patients and other patients in acute care settings have the ability to elicit IgG that binds Type 5 and/or Type 8 capsular polysaccharide of *S. aureus* in an amount sufficient to provide for protection from infection/disease. There is no demonstration of protective immunity or elicitation of antibodies upon administration of the claimed conjugate in humans or in any animal model of correlative of the claimed immune-compromised patients. Such is required by the common meaning as demonstrated by the dictionary definition. As such, one skilled in the art would have ample reasons to doubt the ability to use the claimed composition comprising the glycoconjugates in the absence of further guidance from Applicants with respect to other groups of immune-compromised patients. The courts have held that it is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement. (Genentech Inc. v. Novo Nordisk A/S Ltd., 42 USPQ2d 1001). Moreover, the specification must have been enabling at the time the invention was made and developments after the time of filing are of no consequence to what one skilled in the art would have believed at the time of filing (*In re Wright*, 27 USPQ2d 1510). In the absence of a teaching of the claimed glycoconjugates are effective in generating of sufficient antibody for the prevention of disease in the diverse population of immune-compromised humans, the specification is not be enabled for such. In view of the unpredictability of the art, the lack of teachings of the specification, it would require undue experimentation on the part of the skilled artisan to practice the invention as claimed.

Claims 2 and 3 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

As to claims 2 and 3 the claims are indefinite from the use of the term "conjugate" because the term does not have clear antecedent basis in the independent claim 1. Amendment of the claim to recite "glycoconjugate" would obviate this issue.

Claim Rejections - 35 USC § 102 and 103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 2 is rejected under 35 U.S.C. 102(b) as being clearly anticipated by Welch et al (Journal of the American Society of Nephrology, 7:247-253, 1996; reference A2 on PTOL-1449).

Welch et al teach a method of immunizing end-stage renal disease patients with a *Staphylococcus aureus* composition comprising Type 5 capsular polysaccharide linked to *Pseudomonas aeurgionosa* recombinant exoprotein A (i.e. the instant glycoconjugate) and the antibodies that were induced had opsonophagocytic activity. Because the identical claimed composition was administered to the same patient population, the composition in necessarily and inherently protective. Moreover, the administration of the same composition to the same patient population *in vivo* meets the limitation of the administration as set forth in the art and the administration inherently of the same composition inherently has the claimed functions. Ex parte Novitski 26 USPQ 1389 (BPAI 1993); Mehl/Biophile International Corp. V. Milgraum, 52 USPQ2d 1303 (Fed. Cir. 1999); Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999).

Claims 1, 2, 3, 11, 14, 15 and 17 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Fattom et al, (Annals of Medicine, 28:43-46, 1996; reference A3 on PTOL-1449).

Fattom et al teach that a clinical trial to evaluate the immune response and efficacy indications of a bivalent vaccine in a large population of end-stage renal patients on peritoneal dialysis is underway, with results expected in late 1995. As such, Fattom et al teach the administration of the instantly claimed bivalent type 5 and type 8 conjugate vaccine in end stage renal disease patients in 1995 in this country. Moreover, the administration of the same composition to the same patient population *in vivo* meets the limitation of the administration as set forth in the art and the administration inherently of the same composition inherently has the claimed functions. Ex parte Novitski 26 USPQ 1389 (BPAI 1993); Mehl/Biophile International Corp. V. Milgraum, 52 USPQ2d 1303 (Fed. Cir. 1999); Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999).

Claims 1, 2, 3, 11, 14, 15 and 17 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Vaccine Weekly, September 30, 1996, p 10.

Vaccine Weekly et al teach that StaphVAX™ (*S. aureus* type 5 and 8 capsular polysaccharide conjugate vaccine) was administered to end stage renal disease patients and that it stimulated significant levels of staph fighting antibodies in these patients. The administration of the same composition to the same patient population *in vivo* meets the limitation of the administration as set forth in the art and the administration inherently of the same composition inherently has the claimed functions. Ex parte Novitski 26 USPQ 1389 (BPAI 1993); Mehl/Biophile International Corp. V. Milgraum, 52 USPQ2d 1303 (Fed. Cir. 1999); Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999).

Claims 1, 2, 3, 11, 14 and 15-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fattom et al, (Annals of Medicine, 28:43-46, 1996; reference A3 on PTOL-1449) in view of Grabstein et al (U.S. Patent No. 5,747,024, issued May 5, 1998).

Fattom et al, teach that type 8 CP-rEPA and type 5 CP-rEPA conjugate vaccines were initially evaluated in healthy human volunteers and that both conjugates elicit a 10-20

flod increase in CP-specific antibodies and sera tested provided for oposonophagocytic activity as compared to preimmune sera. Fattom et al teach that the vaccine would be used to prevent staphylococcal infections by *S. aureus* in certain high-risk patient populations such as renal disease patients on dialysis, HIV patients, and individuals with scheduled high-risk surgery who are capable of mounting an immune response are likely to benefit from active immunization. Fattom et al teaches that they began the evaluation of active immunization studies in the target populations and demonstrated that 13 out of 16 hemodialysis patients responded with a 5-fold increase in titer when immunized with the type 5 CP-rEPA alone whereas 23 out of 23 healthy volunteers responded. Fattom et al teach that the data indicate that the conjugate vaccine is immunogenic and can be used for active immunization in some populations, other patient populations may require either higher doses of the vaccine or use of the vaccine with an adjuvant. Fattom et al teach that a clinical trial to evaluate the immune response and efficacy indications of the bivalent *S. aureus* vaccine in a larger population of end-stage renal disease patients on dialysis is underway (page 45, columns 1-2). Fattom et al differs by not administering the bivalent type 5 and type 8 conjugate vaccine to the target population of hemodialysis patients and by not including adjuvants or immune stimulants.

Grabstein et al teach cytokine based immune enhancers/stimulants/adjuvants can be used to enhance a mammals immune response to a vaccine antigen wherein the antigen is combined with IL-15 and G-CSF (see claim 4).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time that the invention was made to administer the bivalent *S. aureus* vaccine in combination with an immune stimulant/enhancer/adjuvant according to Grabstein et al to renal disease patients as directed by Fattom et al because Fattom et al teach that the vaccine is immunogenic in normal individuals, that a trial to evaluate the immune response and efficacy indications of the bivalent *S. aureus* vaccine was underway and Grabstein et al teach that the use of adjuvants would provide for an increased immune response to a

vaccine antigen and Fattom et al teach that other patient populations may require higher dosages of the vaccine or use of an adjuvant to enhance the immune response.

Claims 1, 2, 3, 11, 14 and 15-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fattom et al, (Annals of Medicine, 28:43-46, 1996; reference A3 on PTOL-1449) in view of Fattom et al (Vaccine, 13(14):1288-1293, 1995).

Fattom et al (Annals of Medicine, 28:43-46, 1996; reference A3 on PTOL-1449), teach that type 8 CP-rEPA and type 5 CP-rEPA conjugate vaccines were initially evaluated in healthy human volunteers and that both conjugates elicit a 10-20 fled increase in CP-specific antibodies and sera tested provided for oposonophagocytic activity as compared to preimmune sera. Fattom et al teach that the vaccine would be used to prevent staphylococcal infections by S. aureus in certain high-risk patient populations such as renal disease patients on dialysis, HIV patients, and individuals with scheduled high-risk surgery who are capable of mounting an immune response are likely to benefit from active immunization. Fattom et al teaches that they began the evaluation of active immunization studies in the target populations and demonstrated that 13 out of 16 hemodialysis patients responded with a 5-fold increase in titer when immunized with the type 5 CP-rEPA alone whereas 23 out of 23 healthy volunteers responded. Fattom et al teach that the data indicate that the conjugate vaccine is immunogenic and can be used for active immunization in some populations, other patient populations may require either higher doses of the vaccine or use of the vaccine with an adjuvant. Fattom et al teach that a clinical trial to evaluate the immune response and efficacy indications of the bivalent *S. aureus* vaccine in a larger population of end-stage renal disease patients on dialysis is underway (page 45, columns 1-2). Fattom et al differs by not administering the bivalent type 5 and type 8 conjugate vaccine to the target population of hemodialysis patients and by not including adjuvants or immune stimulants.

Fattom et al (Vaccine, 13(14):1288-1293, 1995) teaches that adjuvants such as monophosphoryl lipid A, QS21 and Novasomes™ were able to increase the antibody levels five fold as compared to the vaccine in the absence of the adjuvant. Significant rises in IgG were observed with all formulations and may prove to be important in immunocompromised patients.

It would have been *prima facie* obvious to one having ordinary skill in the art at the time that the invention was made to administer the bivalent *S. aureus* vaccine in combination with an immune adjuvant according to Fattom et al (Vaccine, 13(14):1288-1293, 1995) to renal disease patients as directed by Fattom et al (Annals of Medicine, 28:43-46, 1996; reference A3 on PTOL-1449) because Fattom et al (Annals of Medicine, 28:43-46, 1996; reference A3 on PTOL-1449) teach that the vaccine is immunogenic in normal individuals, that a trial to evaluate the immune response and efficacy indications of the bivalent *S. aureus* vaccine was underway and Fattom et al (Vaccine, 13(14):1288-1293, 1995) teach that the use of adjuvants would provide for a five fold increased IgG response to a staphylococcal glycoconjugate vaccine antigen and Fattom et al (Annals of Medicine, 28:43-46, 1996; reference A3 on PTOL-1449)teach that other patient populations may require higher dosages of the vaccine or use of an adjuvant to enhance the immune response.

Status of the Claims

Claims 1-3, 11, 12, 14-19 stand rejected. Claims 4-10 and 13 are withdrawn from consideration.

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy whose telephone number is 571-272-0855. The examiner can normally be reached on M-F 6:30 pm - 3:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Smith Lynette can be reached on 571-272-0864.

The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Patricia A. Duffy, Ph.D.

Primary Examiner

Art Unit 1645